REMARKS

Claims 1-33 and 50-61 are pending. Claims 2, 9, 11-12, 14-18, 20, 22-23, 25-26, 30 and 50 were previously withdrawn by the Examiner as being drawn to a non-elected invention. In Applicants response to Office Action dated September 2, 2010, (response filed March 2, 2010), Applicants amended claims 13, 21, 24 and 51 to be directed to methods comprising administering TH2 adjuvant. The Examiner has currently withdrawn claims 13, 21, 24 and 51 as being drawn to a non-elected invention.

Applicants have amended claims 1, 3-8, 10, 13, 19, 21, 27-29, 31-33 and 51 to improve their form. New claims 62-75 have been introduced. Applicants expressly reserve the right to pursue the withdrawn subject matter in a further application that claims priority under 35 U.S.C. § 120 from this application.

Support for the amendments to claims 1, 3-8, 10, 13, 19, 21, 27-29, 31-33 and 51 may be found in the application, as filed, for example previously presented claims 1-51 and at page paragraphs [0064], [0085], [0090] and [0134] of the published application corresponding to U.S. 10/574,393 (US2007/0122417). Additional support for the amendments to the claims is found at paragraphs [0050], [0069]-[0071], [0073] and [0078] of (US2007/0122417). Further support for the claim amendments is found in Examples 1-5.

Applicants assert that no new matter has been entered as a result of the amendments. Applicants request entry of the amendments and reconsideration of the claims.

Applicants thank Examiner Juedes for participating in a telephonic Examiner interview on July 29, 2010. During the interview, the participants discussed rejoinder and examination of claims drawn to administering a TH2 adjuvant (previously withdrawn by the Examiner as being drawn to a non-elected species) upon allowance of a generic claim.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 3-6, 19, 27-28 and 31-33 stand rejected under 35 U.S.C. § 102(b) in view of Franco et al., 1998 ("Franco").

The Examiner asserts at page 2 of the Office Action that Franco "teach a method for reducing TH2 immune response to an antigen comprising administering an antigen via the oral route (i.e. in immunotherapeutic form) and subsequently administering the antigen in CFA by a subcutaneous injection (i.e. in immunogenic form comprising a TH1 adjuvant)".

Applicants respectfully traverse the rejection.

For a prior art reference to anticipate a claimed invention, the prior art must teach ***each and every element*** of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Applicants assert that Franco discloses a method for inducing oral tolerance towards an antigen in unsensitized mice, wherein the method comprises feeding the mice OVA (OVA-DNP) for a number of days and subsequently immunizing the mice by subcutaneous administration of OVA-DNP in CFA (Complete Freund's Adjuvant). Accordingly, the immune system of the mice of the method of Franco is naïve.

Claim 1 and dependent claims thereof require a "an individual sensitized to [an] antigen." Claim 1 also requires a step of "determining that an individual has an immune response when challenged with one or more antigen(s)" prior to the steps of administering the antigen first in an immunotherapeutic form and then in a immunogenic form.

Since the mice of Franco are not sensitized to an antigen prior to immunization and therefore have an immune system that is naïve, the mice of Franco are clearly not "sensitized to [an] antigen" as required by claim 1 and dependent claims thereof. Additionally, Franco does not teach a step of "determining that an individual has an immune response when challenged with one or more antigen(s)" prior to administering an antigen," first in an immunotherapeutic form and then in an immunogenic form, as required by claim 1.

Claims 13, 21 and new claim 62 and dependent claims thereof require "determining that an individual has an antigen specific TH2 immune response when challenged with one or more antigens" or with "an antigen" prior to administering the

antigen, first in an immunotherapeutic form and then in an immunogenic form. As discussed above, since the mice of Franco are not sensitized to an antigen prior to immunization with the antigen they clearly do not have an antigen specific response when challenged with the antigen. In particular, they do not have an "antigen specific TH2 immune response when challenged with one or more antigen(s)" as required by claims 13, 21 and 62. Further, Franco does not teach a step of "determining that an individual has an antigen specific TH2 immune response when challenged with an antigen" prior to administering the antigen first in an immunotherapeutic form and then in an immunogenic form, as required by claims 13, 21 and 62.

Claim 31 requires a step of "determining that an individual has an immune response when challenged with one or more antigen(s)" prior to administration of a plurality of antigen shots. New claim 69 requires "determining that an individual has an immune response when challenged with an antigen" prior to administering the antigen. The mice of Franco are not sensitized to an antigen prior to immunization with the antigen and therefore clearly do not have an immune response when challenged with one or more antigens. Further, Franco does not teach a step of "determining that an individual has an immune response when challenged with one or more antigens" as required by claims 31 and 69.

Applicants assert that the instant specification clearly teaches that the methods of the present invention relate to individuals that are sensitized to an antigen prior to administration of the antigen.

The specification teaches that in one embodiment of the invention an antigen is administered sublingually to desensitize an individual (page 7, paragraph [0100]). Clearly, according to this embodiment, the individual being desensitized must have been previously sensitized to the antigen. Furthermore, an experimental example presented in the specification describes the sensitization of mice prior to the steps of administering an antigen (first in immunotherapeutic form and subsequently in immunogenic form) (Example 5). Moreover, the specification refers to treating an individual "[o]nce an individual afflicted with a TH1 or TH2-associated disease has been diagnosed" (page 6, paragraph [0089]). As such, it is clear from the specification that

the present invention is directed towards administering antigen to individuals sensitized to antigen and, in certain embodiments, individuals that have "an antigen specific TH2 immune response when challenged with an antigen".

Without acquiescing to the rejection and purely to expedite prosecution, claims 1, 13, 21 and 31 have been amended to include an initial step of "determining that an individual has an immune response when challenged with one or more antigen(s)" or "determining that an individual has an antigen specific TH2 immune response" as required by the claims.

Furthermore, treatment according to the method of the present invention results in the down regulation of an immune response to a specific antigen. See, for example, Figures 5-7 (Example 5), which demonstrates that individuals sensitized to OVA and then treated with multiple sublingual doses of OVA before being given an intraperitoneal injection of OVA or OVA and alum had significantly lower anti-OVA IgE antibody levels than individuals sensitized to OVA and then treated with PBS. Conversely, individuals treated according to the method of Franco show an increase in antibody levels after treatment (see Franco, for example, page 4, Figure 1).

Accordingly, while the Examiner correctly asserts that Franco discloses administration of an antigen via an oral route and subsequent administration of the antigen with an adjuvant via subcutaneous injection, in view of the foregoing it is clear that Franco does not teach or suggest "a method of altering a specific immune response to one or more antigen(s) in an individual sensitized to said antigen comprising: i) determining that an individual has an immune response when challenged with one or more antigen(s); ii) administering orally to said individual an effective amount of said antigen(s) in immunotherapeutic form, wherein said administration of said antigen(s) down regulates the immune response; and iii) subsequently administering parenterally to said individual an effective amount of an immunomodifying agent comprising said antigen in immunogenic form" as required by claim 1.

Applicants also assert that Franco does not teach a " method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders,

allergic asthma, atopic dermatitis and allergic rhinitis, said method comprising: i) determining that an individual has an antigen specific TH2 immune response when challenged with an antigen; ii) administering orally to said individual an effective amount of one or more antigen(s) in immunotherapeutic form; and iii) subsequently administering parenterally to said individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen(s) in immunogenic form , wherein said antigen specific TH2 response in said individual is reduced relative to said specific TH2 response before administration of said immunomodifying agent" as required by claim 13.

Applicants submit further that Franco does not teach "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis comprising: i) determining that an individual has an antigen specific TH2 immune response when challenged with one or more antigen(s); ii) administering orally to said individual an effective amount of one or more antigen(s) in immunotherapeutic form, wherein said immune response to said disease is down regulated; and iii) subsequently administering parenterally to said individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen(s) in immunogenic form" as required by claim 21. .

Applicants submit further that Franco does not teach "a method of immunotherapy comprising: i) determining that an individual has an immune response when challenged with one or more antigen(s); ii) administration to said individual a plurality of antigen shots; iii) administration to said individual less than five individual shots of said antigen combined with one or more TH1 and/or TH2 adjuvant(s); wherein the antigen shots of step (ii) are administered orally and the antigen" as required by claim 31.

Applicants submit further that Franco does not teach "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis, said method comprising: i) determining that an individual has an antigen specific TH2 immune response when

challenged with one or more antigen(s); ii) administering orally to said individual an effective amount of said antigen(s) in immunotherapeutic form; and iii) subsequently administering parenterally to said individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen(s) in immunogenic form and a TH2-adjuvant, wherein said antigen specific TH2 response in said individual is reduced relative to the specific TH2 response before administration of said immunomodifying agent" as required by new claim 62.

Applicants submit further that Franco does not teach "a method of treating a TH2-associated disease selected from the group consisting of allergic atopic disorders, allergic asthma, atopic dermatitis and allergic rhinitis comprising: i) determining that an individual has an immune response when challenged with an antigen; ii) administering orally to said individual an effective amount of said antigen in immunotherapeutic form, wherein the immune response to said disease is down regulated; and iii) subsequently administering parenterally to said individual still under the effects of immunotherapy an effective amount of an immunomodifying agent comprising said antigen in immunogenic form and a TH2-adjuvant." as required by claim 69.

As delineated above, Applicants submit that Franco fails to teach each and every element of the claimed subject matter. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Rejections Under 35 U.S.C. § 102(b)

Claims 1, 3-8, 10, 19 and 27-29 stand rejected under 35 U.S.C. § 102(b) in view of Drachenburg et al., 2001 ("Drachenburg"). The Examiner asserts at page 3 of the Office Action that Drachenburg "teach a method of immunotherapy for treating pollen specific allergy comprising administering low doses of pollen allergen and MPL adjuvant (i.e. "immunotherapeutic dose") followed by administration of high doses of pollen allergen and MPL adjuvant (i.e. an "immunogenic" form of the antigen comprising a TH1 adjuvant)".

Applicants respectfully traverse the rejection.

For a prior art reference to anticipate a claimed invention, the prior art must teach

each and every element of the claimed invention. *Lewmar Marine v. Barient*, 827 F.2d 744, 3 USPQ2d 1766 (Fed. Cir. 1987).

Applicants assert that Drachenberg discloses a traditional immunotherapy method, comprising a series of injections with antigen of increasing strength in combination with an adjuvant. Drachenburg does **not** teach a subsequent step of administering "an effective amount of [the] antigen in immunotherapeutic form" as required by claim 1.

The instant specification teaches that an immunogenic form of antigen refers to "a form of or formulation comprising the antigen, which renders the antigen immunogenic" and "also refers to the type of administration and route of administration relative to the type or route of administration used for the immunotherapeutic form of antigen" (see page 7, paragraphs [0099] and [0100] of US 2007/0122417).

To clarify the meaning of an "immunogenic form" of an antigen, as recited in the instant claims, independent claims 1, 13, 21 and 31 have been amended to recite that antigen(s) are initially administered orally (i.e. in immunotherapeutic form), and then administered parenterally (i.e. in immunogenic form).

In view of all of the above, Applicants assert that Drachenburg does not teach "a method of altering a specific immune response to one or more antigen(s) in an individual sensitized to said antigen comprising: i) determining that an individual has an immune response when challenged with one or more antigen(s); ii) administering orally to said individual an effective amount of said antigen(s) in immunotherapeutic form, wherein said administration of said antigen(s) down regulates the immune response; and iii) subsequently administering parenterally to said individual an effective amount of an immunomodifying agent comprising said antigen in immunogenic form" as required by claim 1 and dependent claims thereof.

As delineated above, Applicants submit that Drachenburg fails to teach each and every element of the claimed subject matter. Accordingly, Applicants respectfully request that the rejection under § 102(b) be reconsidered and withdrawn.

For at least the foregoing reasons, each of the presently pending claims in this application is believed to be in condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue. Should any of the claims not be found to be in condition for allowance, the Examiner is requested to call Applicants' undersigned representative to discuss the application. Applicants thank the Examiner in advance for this courtesy.

The Director is hereby authorized to charge or credit any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 04-1105, under Order No. 65138(53253).

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